Endogenous Wnt signaling maintains neural progenitor cell potency.

Journal: Stem Cells

Publication Year: 2009

Authors: Eric M Wexler, Andres Paucer, Harley I Kornblum, Theodore D Palmer, Daniel H Geschwind

PubMed link: 19418460

Funding Grants: Immunology of neural stem cell fate and function

Public Summary:

Scientific Abstract:
Wnt signaling regulates neural stem cell (NSC) function and development throughout an individual's lifetime. Intriguingly, adult hippocampal progenitors (AHPs) produce several Wnts, and the intracellular machinery necessary to respond to them, creating the potential for an active autocrine-signaling loop within this stem cell niche. However, the standard luciferase-based Wnt assay failed to detect this signaling loop. This assay is inherently less temporally sensitive to activity among a population of unsynchronized proliferating cells because it relies on the rapidly degrading reporter luciferase. We circumvented this limitation using a promoter assay that employs green fluorescent protein (GFP), as a relatively long-lived reporter of canonical Wnt activity. We found that at baseline, AHPs secreted functional Wnt that self-stimulates low-level canonical Wnt signaling. Elimination baseline Wnt activity, via application of an extracellular Wnt antagonist promoted neurogenesis, based on a combination of unbiased gene expression analysis and cell-fate analysis. A detailed clonal analysis of progenitors transduced with specific intracellular antagonists of canonical signaling, either Axin or truncated cadherin (beta-catenin sequestering), revealed that loss of baseline signaling depletes the population of multipotent precursors, thereby driving an increasing fraction to assume a committed cell fate (i.e., unipotent progenitors). Similarly, baseline Wnt signaling repressed differentiation of human NSCs. Although the specific Wnts produced by neural precursors vary with age and between species, their effects remain remarkably consistent. In sum, this study establishes that autonomous Wnt signaling is a conserved feature of the neurogenic niche that preserves the delicate balance between NSC maintenance and differentiation.